AMENDMENTS TO THE SPECIFICATION

At page 1, before "Background of Invention", please insert the following paragraph"

--CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Provisional Patent Application Ser. No. 60/410,279, filed on September 13, 2002.--

At Page 10-11 Please replace paragraphs [0050] to [0052] and the included amino acid sequences as follows

[0050] Native HK-D3 has a length of 123 amino acids and a molecular weight of 14007 Da. The amino acid sequence, SEQ ID NO:1, is:

~~1 GKDFVQPPTK ICVGCPRDIP TNSPELEETL THTITKLNAE NNATFYFKID NVKKARVQVV~~
~~61 AGKKYFIDFV ARETTCSKES NEELTESCET KKLGQSLDCN AEVYVVPWEK KIYPTVNCQP~~
~~121 LGM~~

```
Gly Lys Asp Phe Val Gln Pro Pro Thr Lys Ile Cys Val Gly Cys Pro
1               5                  10                  15
Arg Asp Ile Pro Thr Asn Ser Pro Glu Leu Glu Glu Thr Leu Thr His
            20                  25                  30
Thr Ile Thr Lys Leu Asn Ala Glu Asn Asn Ala Thr Phe Tyr Phe Lys
        35                  40                  45
Ile Asp Asn Val Lys Lys Ala Arg Val Gln Val Val Ala Gly Lys Lys
    50                  55                  60
Tyr Phe Ile Asp Phe Val Ala Arg Glu Thr Thr Cys Ser Lys Glu Ser
65                  70                  75                  80
Asn Glu Glu Leu Thr Glu Ser Cys Glu Thr Lys Lys Leu Gly Gln Ser
                85                  90                  95
Leu Asp Cys Asn Ala Glu Val Tyr Val Val Pro Trp Glu Lys Lys Ile
            100                 105                 110
Tyr Pro Thr Val Asn Cys Gln Pro Leu Gly Met
        115                 120
```

[0051] An N-terminal addition variant of HK-D3, designated HK-D3v(GS), that includes an additional Gly Ser sequence at the N-terminus (underscored below) results as a byproduct of the expression system. Its sequence is shown below (SEQ ID NO:2).

~~1 GSGKDFVQPP TKICVGCPRD IPTNSPELEE TLTHTITKLN AENNATFYFK IDNVKKARVQ~~
~~61 VVAGKKYFID FVARETTCSK ESNEELTESC ETKKLGQSLD CNAEVYVVPW EKKIYPTVNC~~
~~121 QPLGM~~

```
Gly Ser Gly Lys Asp Phe Val Gln Pro Pro Thr Lys Ile Cys Val Gly
1               5                  10                  15
Cys Pro Arg Asp Ile Pro Thr Asn Ser Pro Glu Leu Glu Glu Thr Leu
```

```
            20                  25                  30
Thr His Thr Ile Thr Lys Leu Asn Ala Glu Asn Asn Ala Thr Phe Tyr
        35                  40                  45
Phe Lys Ile Asp Asn Val Lys Lys Ala Arg Val Gln Val Val Ala Gly
    50                  55                  60
Lys Lys Tyr Phe Ile Asp Phe Val Ala Arg Glu Thr Thr Cys Ser Lys
65                  70                  75                  80
Glu Ser Asn Glu Glu Leu Thr Glu Ser Cys Glu Thr Lys Lys Leu Gly
                85                  90                  95
Gln Ser Leu Asp Cys Asn Ala Glu Val Tyr Val Val Pro Trp Glu Lys
            100                 105                 110
Lys Ile Tyr Pro Thr Val Asn Cys Gln Pro Leu Gly Met
        115                 120                 125
```

[0051] Another variant of HK-D3, designated HK-D3v (shown below as SEQ ID NO:3), which the present inventors cloned and expressed and tested in the Examples below, has a length of 127 amino acids and a molecular weight of 14409 Da. First, the N-terminal G and S are not part of the native HK-D3 sequence. The additions at the N-terminus and replacements/additions at the C-terminus are underscored.

~~1 *GS*GKDFVQPP TKICVGCPRD IPTNSPELEE TLTHTITKLN AENNATFYFK IDNVKKARVQ~~
~~61 VVAGKKYFID FVARETTCSK ESNEELTESC ETKKLGQSLD CNAEVYVVPW EKKIYPTVTV~~
~~121 NHWECEF~~ **SEQ ID NO:3**

```
Gly Ser Gly Lys Asp Phe Val Gln Pro Pro Thr Lys Ile Cys Val Gly
1               5                   10                  15
Cys Pro Arg Asp Ile Pro Thr Asn Ser Pro Glu Leu Glu Glu Thr Leu
            20                  25                  30
Thr His Thr Ile Thr Lys Leu Asn Ala Glu Asn Asn Ala Thr Phe Tyr
        35                  40                  45
Phe Lys Ile Asp Asn Val Lys Lys Ala Arg Val Gln Val Val Ala Gly
    50                  55                  60
Lys Lys Tyr Phe Ile Asp Phe Val Ala Arg Glu Thr Thr Cys Ser Lys
65                  70                  75                  80
Glu Ser Asn Glu Glu Leu Thr Glu Ser Cys Glu Thr Lys Lys Leu Gly
                85                  90                  95
Gln Ser Leu Asp Cys Asn Ala Glu Val Tyr Val Val Pro Trp Glu Lys
            100                 105                 110
Lys Ile Tyr Pro Thr Val Thr Val Asn His Trp Glu Cys Glu Phe
        115                 120                 125
```

At page 12-13: Please replace Paragraph [0061] as follows *{to kill a hyperlink}*:

[0061] The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (J. Mol. Biol. 48:444-453 (1970) algorithm which has been incorporated into the GAP program in the GCG software package (available at ~~http://www.~~ The World Wide Web URL: gcg.com), using either a Blossom 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at the website having the URL "gcg.com", using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Meyers et al. (CABIOS, 4:11-17 (1989)) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

At page 16: Please replace Paragraph [0074] as follows: *{to remove extraneous characters}*

[0074] The polypeptides of the invention are preferably be prepared using recombinant DNA technology although they may also be prepared using solid-phase synthesis [[???]], such as that generally described by Merrifield, J. Amer. Chem. Soc., 85:2149-54 (1963), although other equivalent chemical syntheses known in the art are also useful. Solid-phase peptide synthesis may be initiated from the C-terminus of the peptide by coupling a protected α-amino acid to a suitable resin. Such a starting material can be prepared by attaching an α-amino-protected amino acid by an ester linkage to a chloromethylated resin or to a hydroxymethyl resin, or by an amide bond to a BHA resin or MBHA resin. Such methods, well-known in the art, are disclosed, for example, in U.S. Pat. 5,994,309 which is incorporated by reference in its entirety.

At page 17: Please replace Paragraph [0078] as follows *{to add a missing ")"}*:

[0078] The nucleotide sequence (SEQ ID NO:4) and amino acid sequence (SEQ ID NO:1) of HK-D3 are derived from the sequence of the full length HK protein and DNA or shorter fragments that are available from GenBank (e.g., GenBank Accession number AH005302 and Swiss Prot number: P01042).

At page 36: Please replace Paragraph [0146] as follows *{to add a missing "("}*:

[0146] Lectins are proteins, commonly derived from plants, that bind to carbohydrates. Among other activities, some lectins are toxic. Some of the most cytotoxic substances known are protein toxins of bacterial and plant origin (Frankel, AE et al., Ann. Rev. Med. 37:125-142 (1986)). These molecules binding the cell surface and inhibit cellular protein synthesis. The most commonly used plant toxins are ricin and abrin; the most commonly used bacterial toxins are diphtheria toxin and Pseudomonas exotoxin A. In ricin and abrin, the binding and toxic functions are contained in

two separate protein subunits, the A and B chains. The ricin B chain binds to the cell surface carbohydrates and promotes the uptake of the A chain into the cell. Once inside the cell, the ricin A chain inhibits protein synthesis by inactivating the 60S subunit of the eukaryotic ribosome (Endo, Y. et al., J. Biol. Chem. 262: 5908-5912 (1987)). Other plant derived toxins, which are single chain ribosomal inhibitory proteins, include pokeweed antiviral protein, wheat germ protein, gelonin, dianthins, momorcharins, trichosanthin, and many others (Strip, F. et al., FEBS Lett. 195:1-8 (1986)). Diphtheria toxin and Pseudomonas exotoxin A are also single chain proteins, and their binding and toxicity functions reside in separate domains of the same protein Pseudomonas exotoxin A has the same catalytic activity as diphtheria toxin. Ricin has been used therapeutically by binding its toxic α-chain, to targeting molecules such as antibodies to enable site-specific delivery of the toxic effect. Bacterial toxins have also been used as anti-tumor conjugates. As intended herein, a toxic peptide chain or domain is conjugated to a compound of this invention and delivered in a site-specific manner to a target site where the toxic activity is desired, such as a metastatic focus. Conjugation of toxins to protein such as antibodies or other ligands are known in the art (Olsnes, S. et al., Immunol. Today 10:291-295 (1989); Vitetta, ES et al., Ann. Rev. Immunol. 3:197-212 (1985)).

At page 47-48: Please replace Paragraph [0196] as follows {*to add a missing ")"*}:

[0196] A promoter region of a DNA or RNA molecule binds RNA polymerase and promotes the transcription of an "operably linked" nucleic acid sequence. As used herein, a "promoter sequence" is the nucleotide sequence of the promoter which is found on that strand of the DNA or RNA which is transcribed by the RNA polymerase. The preferred promoter sequences of the present invention must be operable in mammalian cells and may be either eukaryotic or viral promoters. Although preferred promoters are described in the Examples, other useful promoters and regulatory elements are discussed below. Suitable promoters may be inducible, repressible or constitutive. A "constitutive" promoter is one which is active under most conditions encountered in the cell's environmental and throughout development. An "inducible" promoter is one which is under environmental or developmental regulation. A "tissue specific" promoter is active in certain tissue types of an organism. An example of a constitutive promoter is the viral promoter MSV-LTR, which is efficient and active in a variety of cell types, and, in contrast to most other promoters, has the same enhancing activity in arrested and growing cells. Other preferred viral promoters include that present in the CMV-LTR (from cytomegalovirus) (Bashart, M. et al., Cell 41:521 (1985)) or in the RSV-LTR (from Rous sarcoma virus) (Gorman, CM, Proc. Natl. Acad. Sci. USA 79:6777 (1982)). Also useful are the promoter of the mouse metallothionein I gene (Hamer, D., et al., J. Mol. Appl. Gen. 1:273-288 (1982)); the TK promoter of Herpes virus (McKnight, S., Cell 31:355-365 (1982)); the SV40 early promoter (Benoist, C., et al., Nature 290:304-310 (1981)); and the yeast gal4 gene promoter (Johnston, SA, et al., Proc. Natl. Acad. Sci. (USA) 79:6971-6975 (1982); Silver, PA, et al., Proc. Natl. Acad. Sci. (USA) 81:5951-5955 (1984)). Other illustrative descriptions of transcriptional factor association with promoter regions and the separate activation and DNA binding of transcription factors include: Keegan et al., Nature (1986) 231:699; Fields et al., Nature (1989)

340:245; Jones, Cell (1990) 61:9; Lewin, Cell (1990) 61:1161; Ptashne et al., Nature (1990) 346:329; Adams et al., Cell (1993) 72:306. The relevant disclosure of all of these above-listed references is hereby incorporated by reference.

At page 50-51: Please replace Paragraph [0204] as follows {*to add 3 ")" and delete errant ","*}:

[0204] Retroviral-mediated human therapy utilizes amphotrophic, replication-deficient retrovirus systems (Temin, HM, Human Gene Therapy 1:111 (1990); Temin et al., U.S. Patent 4,980,289; Temin et al., U.S. Patent 4,650,764; Temin et al., U.S. Patent No. 5,124,263; Wills, JW, U.S. Patent 5,175,099; Miller, AD, U.S. Patent No. 4,861,719). Such vectors have been used to introduce functional DNA into human cells or tissues, for example, the adenosine deaminase gene into lymphocytes, the NPT-II gene and the gene for tumor necrosis factor into tumor infiltrating lymphocytes. Retrovirus-mediated gene delivery generally requires target cell proliferation for gene transfer (Miller, DG et al., Mol. Cell. Biol. 10:4239 (1990)). This condition is met by certain of the preferred target cells into which the present DNA molecules are to be introduced, i.e., actively growing tumor cells. The DNA molecules encoding the HK-D3 polypeptide of the present invention may be packaged into retrovirus vectors using packaging cell lines that produce replication-defective retroviruses, as is well-known in the art (see, for example, Cone, RD et al., Proc. Natl. Acad. Sci. USA 81:6349-6353 (1984); Mann, RF et al., Cell 33:153-159 (1983); Miller, AD et al., Molec. Cell. Biol. 5:431-437 (1985)[[,]]; Sorge, J., et al., Molec. Cell. Biol. 4:1730-1737 (1984); Hock, RA et al., Nature 320:257 (1986); Miller, AD et al., Molec. Cell. Biol. 6:2895-2902 (1986)). Newer packaging cell lines which are efficient an safe for gene transfer have also been described (Bank et al., U.S. 5,278,056).

At page 50-51: Please replace Paragraph [0206] as follows {*to correct several typos*}:

[206] Other virus vectors may also be used, including recombinant adenoviruses (Horowitz, MS, In: Virology, Fields, BN et al., eds, Raven Press, New York, 1990, p. 1679; Berkner, KL, Biotechniques 6:616-629, [[919]]1988), Strauss, SE, In: The Adenoviruses, Ginsberg, HS, ed., Plenum Press, New York, 1984, chapter 11), herpes simplex virus (HSV) for neuron-specific delivery and persistence. Advantages of adenovirus vectors for human gene delivery include the fact that recombination is rare, no human malignancies are known to be associated with such viruses, the adenovirus genome is double stranded DNA which can be manipulated to accept foreign genes of up to 7.5 kb in size, and live adenovirus is a safe human vaccine organisms. Adeno-associated virus is also useful for human therapy (Samulski, RJ et al., EMBO J. 10:3941 (1991)) in the present invention.